

-159-

include Cisplatin, actinomycin D, 5-fluorouracil, bleomycin, and cyclophosphamide methotrxate.

In the treatment of superficial bladder cancer, COX-2 inhibitors can be used to treat the disease in
5 combination with other COX-2 inhibitors, or in combination with surgery (TUR), chemotherapy and intravesical therapies.

A preferred therapy for the treatment of superficial bladder cancer is a combination of
10 therapeutically effective amounts of one or more COX-2 inhibitors in combination with: thiotepa (30 to 60 mg/day), mitomycin C (20 to 60 mg/day), and doxorubicin (20 to 80 mg/day).

A preferred intravesicle immunotherapeutic agent
15 that may be used in the present invention is BCG. A preferred daily dose ranges from 60 to 120 mg, depending on the strain of the live attenuated tuberculosis organism used.

A preferred photodynamic therapeutic agent that may
20 be used with the present invention is Photofrin I, a photosensitizing agent, administered intravenously. It is taken up by the low-density lipoprotein receptors of the tumor cells and is activated by exposure to visible light. Additionally, neomydium YAG laser activation
25 generates large amounts of cytotoxic free radicals and singlet oxygen.

In the treatment of muscle-invasive bladder cancer, COX-2 inhibitors can be used to treat the disease in
combination with other COX-2 inhibitors, or in
30 combination with surgery (TUR), intravesical

-160-

chemotherapy, radiation therapy, and radical cystectomy with pelvic lymph node dissection.

A preferred radiation dose for the treatment of bladder cancer is between 5,000 to 7,000 cGY in 5 fractions of 180 to 200 cGY to the tumor. Additionally, 3,500 to 4,700 cGY total dose is administered to the normal bladder and pelvic contents in a four-field technique. Radiation therapy should be considered only if the patient is not a surgical candidate, but may be 10 considered as preoperative therapy.

A preferred combination of surgery and chemotherapeutic agents that can be used in combination with the COX-2 inhibitors of the present invention is cystectomy in conjunction with five cycles of cisplatin 15 (70 to 100 mg/m²); doxorubicin (50 to 60 mg/m²); and cyclophosphamide (500 to 600 mg/m²).

A more preferred therapy for the treatment of superficial bladder cancer is a combination of 20 therapeutically effective amounts of one or more COX-2 inhibitors.

An even more preferred combination for the treatment of superficial bladder cancer is a combination of therapeutically effective amounts of one or more COX- 25 2 inhibitors in combination with the following combinations of antineoplastic agents: 1) cisplatin, doxorubicin, cyclophosphamide; and 2) cisplatin, 5-fluorouracil. An even more preferred combination of chemotherapeutic agents that can be used in combination 30 with radiation therapy and the COX-2 inhibitors is a combination of cisplatin, methotrexate, vinblastine.

-161-

Currently no curative therapy exists for metastatic bladder cancer. The present invention contemplates an effective treatment of bladder cancer leading to improved tumor inhibition or regression, as compared to
5 current therapies.

In the treatment of metastatic bladder cancer, COX-2 inhibitors can be used to treat the disease in combination with other antiangiogenic agents, or in combination with surgery, radiation therapy or with
10 chemotherapeutic agents.

A preferred therapy for the treatment of metastatic bladder cancer is a combination of therapeutically effective amounts of one or more COX-2 inhibitors.

A more preferred combination for the treatment of
15 metastatic bladder cancer is a combination of therapeutically effective amounts of one or more COX-2 inhibitors in combination with the following combinations of antineoplastic agents: 1) cisplatin and methotrexate; 2) doxorubicin, vinblastine,
20 cyclophosphamide, and 5-fluorouracil; 3) vinblastine, doxorubicin, cisplatin, methotrexate; 4) vinblastine, cisplatin, methotrexate; 5) cyclophosphamide, doxorubicin, cisplatin; 6) 5-fluorouracil, cisplatin.

25 Example 6

Pancreas Cancer

Approximately 2% of new cancer cases diagnoses in the United States is pancreatic cancer. Pancreatic
30 cancer is generally classified into two clinical types: 1) adenocarcinoma (metastatic and non-metastatic), and